Study protocol

A single-center, assessor-blinded, randomized-controlled feasibility study of near infrared spectroscopy neurofeedback for binge-eating disorder

NIRSBED

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CONTENT

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Protocol synopsis

Title of the study:	Near Infrared Spectroscopy Neurofeedback for Binge-Eating Disorder (NIRSBED)
Abbreviation of the study:	NIRSBED
Condition:	Binge-eating disorder (BED)
Primary objective of the study:	Efficacy of functional near infrared spectroscopy (fNIRS) neurofeedback in the treatment of adult binge-eating disorder
Secondary objective of the study:	Feasibility of fNIRS neurofeedback including recruitment, attrition, assessment completion, patients' program evaluation, and efficacy on eating disorder psychopathology, executive functioning, weight loss maintenance behavior, and mental and physical health Determining the specificity of efficacy of fNIRS neurofeedback via comparison with active and inactive control conditions
Study design:	Single-center, assessor-blinded, randomized-controlled, three-armed, feasibility study
Study population:	Inclusion criteria: - Ages ≥ 18 years - Full syndrome binge-eating disorder (BED) or BED of low frequency and/or limited duration according to DSM-5 - BMI: 25.0 - 45.0 kg/m^2 - Written informed consent - Sufficient German language skills - Feasible commute to the IFB Research Unit Exclusion criteria: - Serious somatic conditions (e.g., neurological disorders, stroke, head injury) - Serious mental disorders (e.g., psychotic disorder, suicidality, substance use disorder, ADHD, developmental or intellectual disability) - Impediment in hearing, vision, or language with an effect on testing - Previous or planned bariatric surgery - Use of medication that impacts weight or executive functioning (e.g., antipsychotics) - Ongoing psychotherapy - Pregnancy or lactation
Sample size:	N = 78, n = 26 per study arm
Therapy:	Experimental intervention: 12 sessions (60 min) over 8 weeks of fNIRS neurofeedback treatment focusing on food-related self-regulation for improving binge eating and associated psychopathology, executive functions, weight loss maintenance behavior, and mental and physical health.

	Control intervention (1): 12 sessions (60 min) over 8 weeks of electroencephalography (EEG) neurofeedback (high beta training) Control (2): 8 weeks without treatment, after which 12 sessions (60 min) over 8 weeks of fNIRS neurofeedback will be offered (delayed treatment control condition)
Primary outcome:	The number of objective binge-eating episodes (OBEs) over the past 14 days at post-treatment (t1), derived from the Eating Disorder Examination, will be compared between groups, correcting for the baseline value
Secondary outcome:	- Feasibility including recruitment, attrition, assessment completion, patients' program evaluation - Eating disorder psychopathology - Executive functioning - Weight management behavior - Mental and physical health
Biometry:	Efficacy / test accuracy: The comparison between the groups with respect to binge eating episodes directly after treatment. Safety: Report of type and frequency of adverse events. Secondary endpoints: Descriptive analyses, effect sizes, presented with 95% confidence intervals, parametric or non-parametric tests, regression analyses.
Trial duration:	Duration of intervention per patient: 8 weeks Follow-up per patient: 6 months First patient in to last patient out (months): 25 months Duration of the entire trial (months): 30 months Recruitment period (months): 17 months

Flow chart

Patients in behavioral weight loss treatment at the IFB Outpatient Unit will be informed about the study and screened for inclusion. Additionally, patients will be recruited from other clinical settings or from the community. Eligible patients will be invited to attend a diagnostic session. After establishing inclusion, patients will be randomized to one of the three study arms. Assessment time points are at: pre-treatment (t0), post-treatment (t1), and 6-month follow-up (t2) for binge eating, executive functions (t0 and t1 only), weight management-related behavior, as well as mental and physical health.

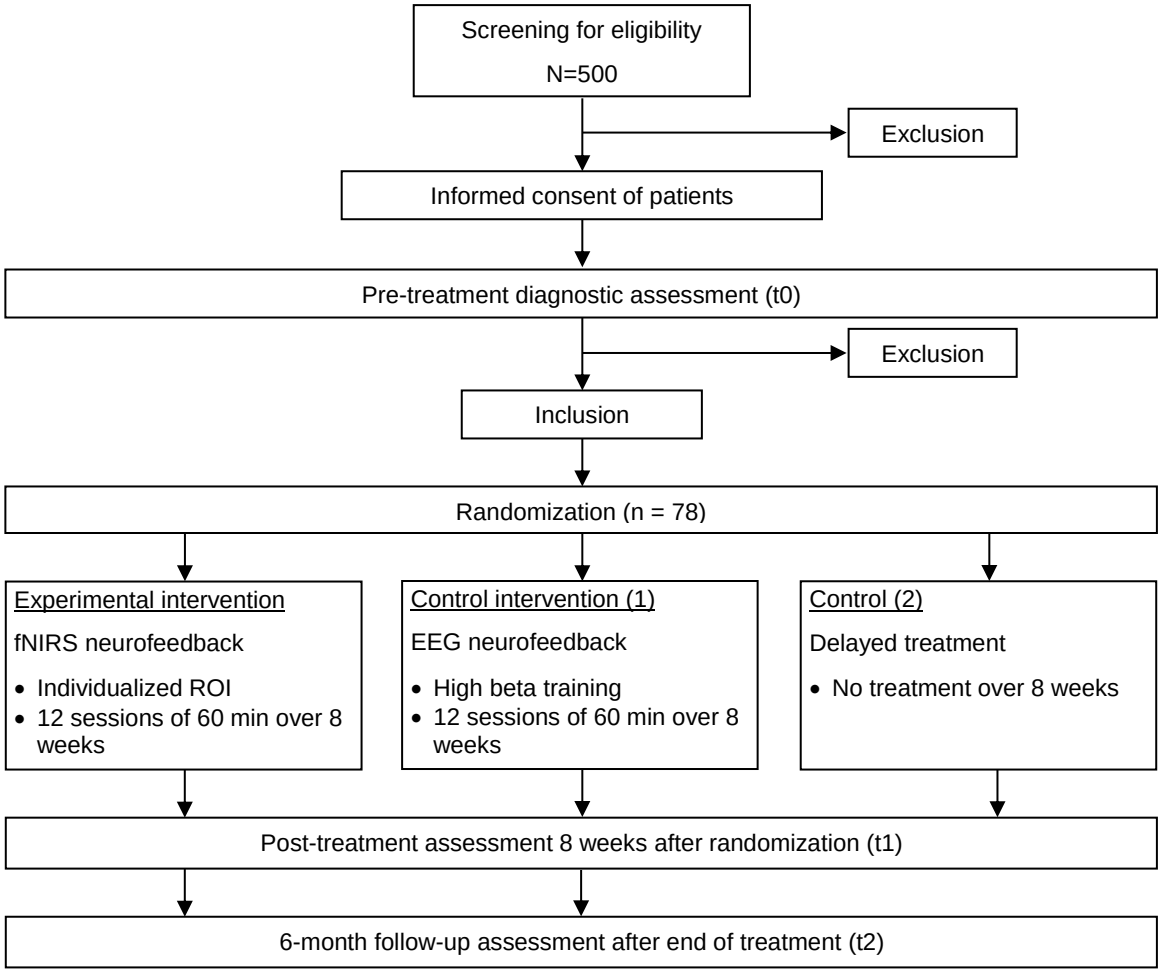

Figure 1. Study flow chart

Assessment	**Screening**	**Therapy**				**Follow-up**
	Before randomization	**Baseline (t0)**	**Only WL Before start of therapy**	**Weekly during therapy**	**End of therapy (t1)**	**After end of therapy (t2)**
Active treatment arms	**-14 – -1 days**	**week 0**	**-**	**week 1-7**	**week 8**	**6 months**
Waiting-list (WL) control	**-14 – -1 days**	**week 0**	**week 8**	**week 9-15**	**week 16**	
Consent form		●				
Anamnesis		●	●			
Comorbidities		●	●		●	
Medication intake		●	●		●	
Inclusion and exclusion criteria	●	●				
Randomisation		●				
Anthropometry		●	●		●	●
Weight and height measure		●	●		●	●
Sociodemography		●	●		●	●
Eating disorder psychopathology		●	●		●	●
General psychopathology		●	●		●	●
Executive functions		●			●	●
Neuropsychological tasks		●	●		●	
Behavioral measures		●	●		●	●
Believed group assignment					●	
Visual analogue scales (VAS): expectations, motivation, and treatment evaluation		●	●		●	

Assessment	**Screening**	**Therapy**				**Follow-up**
	Before randomization	**Baseline (t0)**	**Only WL Before start of therapy**	**Weekly during therapy**	**End of therapy (t1)**	**After end of therapy (t2)**
Active treatment arms	**-14 – -1 days**	**week 0**	**-**	**week 1-7**	**week 8**	**6 months**
Waiting-list (WL) control	**-14 – -1 days**	**week 0**	**week 8**	**week 9-15**	**week 16**	
Brain activity-related outcomes		●		●	●	
Visual analogue scales (VAS): state craving, liking, sense of control, hunger, satiety, and mood		●		●	●	
(Serious) adverse events				●	●	

1 RATIONALE AND RESEARCH QUESTION

1.1 Background

Binge-eating disorder (BED) is characterized by recurrent binge eating, defined as eating a large amount of food accompanied by a sense of loss of control over eating which occurs in the absence of regular inappropriate compensatory behaviors to prevent weight gain.[1] BED is reliably associated with increased eating disorder and general psychopathology, significant distress, lowered quality of life, and overweight and obesity. With prevalence rates of 1.9% in the adult population[2] and of up to 30% in adults with obesity seeking behavioral weight loss (BWL) treatment,[3] BED is the most prevalent eating disorder. As compiled in systematic reviews, meta-analyses, and clinical treatment guidelines,[4–7] psychotherapy is considered to be the first-line treatment of BED, leading to large and long-lasting improvements in binge eating and remission rates of about 50% of patients, while body weight is stabilized. In contrast, BWL treatment yields greater weight loss, but low weight loss maintenance (WLM), and decreased long-term efficacy regarding binge eating.[8] These results underline the necessity of further improving long-term outcome of these patients.

Binge eating and difficulties with WLM in BED are likely related to underlying neurobehavioral difficulties, including an increased impulsivity, low inhibitory control, decreased interoceptive ability, and hyper-responsivity to reward, especially in the processing of disorder-related stimuli such as food cues, while general impairments were not consistently found.[9–12] Using eye-tracking, individuals with BED showed greater maintained attention to – and facilitated search of – food cues than weight-matched controls.[13,14] Neuropsychological tasks revealed inhibitory deficits with regards to food cues (e.g., Go/no-Go),[15,16] and a steeper delay discounting in individuals with BED than in weight-matched controls.[17] Using electro-encephalography (EEG), individuals with BED showed larger long-latency event-related potentials for high caloric food pictures compared to weight-matched controls, while no differences were observed for low caloric food pictures.[18] Higher frontal beta activity was found in response to food stimuli compared with control stimuli for both individuals with BED and weight-matched controls;[19] independent of the stimulus, the resting state frontal beta activity was greater in individuals with BED. Functional magnetic resonance imaging (fMRI) studies documented a differential activation in areas related to food-related inhibitory control and reward processing.[9–11] For example, hypoactivity in prefrontal networks related to decreased response inhibition was found that occurred especially in response to food cues in individuals with BED when compared to weight-matched controls,[20] and a greater activation in the medial orbito-frontal cortex was found in response to food cues when compared to overweight and normal weight controls.[21] Using Positron Emission Tomography (PET), dopamine release was increased in the dorsal striatum in response to food stimuli in obese individuals with BED, but not in obese controls.[22] Overall, these results support difficulties in inhibitory control and reward processing in BED, with similarities to other neurobehavioral disorders such as attention deficit-/hyperactivity disorder (ADHD) and substance use disorder.[23,24]

In order to specifically target these neurobehavioral difficulties, brain-directed treatments for BED are being developed.[25,26] Neurofeedback – a form of biofeedback – is one brain-directed approach with most of its empirical support in the treatment of ADHD,[27] and initial evidence in substance use disorder.[28] In EEG neurofeedback treatment, participants learn to regulate their brain activity (e.g., downregulate high beta activity), using online feedback through a brain-computer interface and operant conditioning. Initial evidence exists on the efficacy of EEG neurofeedback using food stimuli to reduce overeating tendencies in subclinical samples of restrained eaters.[29–31] While EEG neurofeedback has several clear advantages, such as low cost, high portability, and high disseminability into clinical practice, the resolution is lower than with neurofeedback based on functional imaging methods, theoretically allowing for training of circumscribed brain areas. Proof-of-concept studies are emerging for real-time fMRI

neurofeedback using food cues in healthy individuals;[26,33] however, evidence for clinical populations including BED is lacking, and related to high cost, its disseminability into clinical practice is questionable.

A novel, potentially disseminable, portable, and low-cost method suited to address cortical aspects of neurobehavioral difficulties is functional near-infrared spectroscopy (fNIRS), an optical imaging method, which allows for noninvasive in vivo measurement of changes in the concentration of oxygenated and deoxygenated hemoglobin in brain tissue.[34–36] fNIRS has repeatedly been crossvalidated, for example, against fMRI,[37,38] confirming the physiological basis of the signal. In ADHD, a controlled pilot study (N = 27) showed that after 12 sessions of fNIRS neurofeedback, 7-10 year old children learned to self-regulate brain activity on the basis of the relative oxygenated hemoglobin in the dorsolateral prefrontal cortex and revealed significantly decreased ADHD symptoms at posttreatment and 6-month follow-up.[39] In contrast, the control treatments, EEG neurofeedback (slow cortical potentials) and EMG feedback (musculus supraspinatus), only showed significant changes at 6-month follow-up, thus supporting a faster change with fNIRS neurofeedback.[40] As fNIRS is relatively easy to apply (no fixation of electrodes), insensitive to motion artifacts, and allows measurements to be performed in a natural sitting position, it might provide a valuable alternative to EEG for neurofeedback training in BED. While fNIRS studies in individuals with BED have not been conducted, research in other clinical eating disorders and obesity is sparse.[41–44]

1.2 Rationale

1.2.1 Hypotheses and experimental aspects of the clinical trial

Given the need to further improve treatment outcome for BED, new treatments should address underlying neurobehavioral difficulties such as low inhibitory control. Based on the initial evidence on neurofeedback described above, investigation of fNIRS neurofeedback in adults with BED is a logical next step of research. Improved self-regulation likely has an impact on weight management; in fact, binge eating is a negative prognostic indicator for long-term WLM.[45,46] Thus, the goal of this randomized-controlled trial (RCT) is to evaluate the feasibility and efficacy of fNIRS neurofeedback in patients with BED and overweight or obesity. It is hypothesized that fNIRS neurofeedback will be feasible and estimates regarding efficacy will be better than for delayed treatment control. The number of objective binge-eating episodes (OBEs) over the past 14 days at post-treatment (t1), derived from the Eating Disorder Examination, will be compared between groups, correcting for the baseline value.[56] OBEs are consistently reported as the primary outcome measure in BED treatment trials.[7] In order to address the specific mechanisms of action, fNIRS neurofeedback will further be compared to EEG neurofeedback. As BED and the associated comorbidities increase direct and indirect societal costs beyond those of obesity alone,[47,48] fNIRS neurofeedback has the potential to produce a reduction of these costs. In Germany and internationally, evaluations of fNIRS treatment approaches in BED are lacking. It is thus a clinical and research priority to examine the feasibility and efficacy of fNIRS neurofeedback for adults with BED.

Intervention. *fNIRS neurofeedback:* The fNIRS neurofeedback training will be delivered in 12 individual sessions (60 min) over 8 weeks. Personally salient binge food stimuli (and matched neutral stimuli, i.e., household items) will be pre-selected from validated databases.[49,50] The fNIRS neurofeedback protocol will include a *localization trial* at the outset, during which the individual target area in the prefrontal cortex (e.g., dorsolateral, orbitofrontal)[52] that demonstrates reliable activation differences in response to food stimuli compared to rest, will be selected for training (region of interest, ROI). Detailed working instructions will be derived from pilot measurements. The localization trial will include a rest period, a perceptual food cue exposure (“watch”), a craving food cue exposure (“allow yourself to crave”), and a perceptual neutral cue exposure (household items). The *neurofeedback trials* will include a rest period and regulation food cue exposure (“reduce craving”), followed by rest and reinforcement. During food cue exposure, each food cue

is presented with variable size according to the change in percent blood oxygenation level dependent signal, relative to the preceding fixation block.[33,53] The goal is to reduce craving by decreasing the size of the food cue. For optimal learning, cognitive-behavioral techniques will be used such as information, reinforcement and self-reinforcement, guided discovery of self-regulation skills, cognitive restructuring, goal setting and planning of transfer into daily life, and homework assignments.[54]

Control. Two control conditions will be used: (1) *EEG neurofeedback:* A validated food cue-based EEG training protocol (high beta training)[32] will be used with 12 individual sessions (60 min) over 8 weeks. This condition serves to examine the comparative efficacy and specificity of changes. (2) *Delayed treatment control condition:* The untreated group will not receive any treatment over 8 weeks, but will afterwards be offered fNIRS neurofeedback. This control condition is essential for examining basic efficacy.

1.3 Benefit-risk ratio

In case of randomization to either intervention condition, the major benefit will be a decrease of OBEs, likely resulting in an improvement of long-term weight management and alleviation of obesity-related morbidity. Patients in the delayed treatment control arm will be offered fNIRS neurofeedback treatment afterwards. Patients will not incur any costs for participation. There are no serious health risks known to be associated with neurofeedback programs.[39,40,55] The reported adverse events plateaued at transient mental fatigue and physical discomfort. Written informed consent will be obtained prior to randomization. The patients can withdraw at any time point without any disadvantage. Confidentiality of patients' data will be protected by a documentation system working with anonymous patient codes.

Ethical approval of the study will be sought at the Ethics Committee of the University of Leipzig. The trial will be conducted in accordance with the guidelines for Good Clinical Practice (GCP). All study staff commit themselves to the Declaration of Helsinki (Version Sommerset West 1996), as well as all pertinent national laws and the ICH guidelines for GCP issued in June 1996 and CPMP/ICH/ 135/95 from September 1997.

2 STUDY OBJECTIVES

2.1 Primary outcome

The number of objective binge-eating episodes (OBEs) over the past 14 days at post-treatment (t1), derived from the well-established Eating Disorder Examination[56], will be compared between groups, correcting for the baseline value. OBEs are consistently reported as the primary outcome measure in BED treatment trials.[7] It will be determined whether neurofeedback results in a significantly lower number of OBEs over the past 14 days at post-treatment (t1) compared to the delayed control intervention and how fNIRS, EEG, and delayed control intervention compare.

2.2 Secondary outcomes

Secondary objectives include the evaluation of the following parameters for group and temporal comparisons.

(a) Feasibility (between t0-t1): Recruitment, attrition, assessment completion, compliance, patients' program evaluation

(b) Number of OBEs (t0, t2), remission from objective binge eating (EDE), eating disorder psychopathology (EDE-Q) (t0-t2)

(c) Neuropsychological and brain-activity-related outcomes (t0, t1): e.g., inhibition (Go/NoGo task)

(d) Weight management-related behaviors (t0-t2): e.g., self-efficacy (GSES)

(e) Mental health (t0-t2): e.g., depressive symptoms (PHQ-D)

(f) Physical health (t0-t2): e.g., body mass index (kg/m^2)

3 STUDY DESCRIPTION

3.1 Study design

This is a single-center, assessor-blinded, randomized-controlled, three-armed, feasibility study of fNIRS neurofeedback for BED.

3.2 Personal und technical requirement

This study is led by Prof. Dr. Anja Hilbert in collaboration with the IFB Outpatient Unit and involves a research team with experience in neurophysiological research, assessments, and treatments, including MSc- and PhD-level clinical psychologists. All assessments will be conducted by trained assessors, blind to study hypotheses and randomization. All study personnel will undergo extensive training and will receive ongoing supervision. Office space will be provided at the Red House (Rotes Haus). The IFB Research Unit (led by Prof. Dr. Anja Hilbert) offers a NIRS device, an EEG neurofeedback device, a neuropsychological test battery, laboratory space as well as individual interview facilities.

3.3 Participating center(s) and sample size

Within this single center study, patient recruitment will be based on the IFB Outpatient Unit. Additionally, patients from other clinical settings and from the community will be recruited. A total of N = 78 patients will be included. To attain the total sample size, 500 patients will need to be screened over the 17-month recruitment period in order to determine eligibility.

3.4 Proposed study duration

Study duration per patient will be 10 months at most.

- fNIRS neurofeedback/ EEG neurofeedback: 8 weeks (+ max. 2 weeks) treatment (+ 2 max. weeks assessment range) + 6-month follow-up (+ max. 2 weeks assessment range)
- Delayed intervention control condition:

  8 weeks no treatment (max. 2 weeks assessment range) + 8 weeks (+ max. 2 weeks) treatment (+ max. 2 weeks assessment range) + 6-month follow-up (+ 2 max. weeks assessment range)

The duration of the entire trial is 30 months.

- Study preparations (assessments, therapist training, etc.): 6 months
- Recruitment period: 17 months
- First patient in to last patient out: 25 months (17 months recruitment + 2 months intervention + 6 months follow-up)

3.5 Premature termination of the trial

3.5.1 Termination of the trial

The responsible investigator has the right to discontinue the trial

- if information emerges that affects the benefit/risk ratio of the trial;
- if actual recruitment and follow-up rates do not guarantee the necessary statistical power;
- if there are repeated serious adverse events (SAE) presumably associated with the trial.

4 STUDY POPULATION

4.1 Inclusion criteria

- Ages ≥ 18 years
- BED or BED of low frequency and/or limited duration as established according to DSM-5
- BMI 25.0 - 45.0 kg/m^2
- Written informed consent
- Sufficient German language skills
- Feasible commute to the IFB Research Unit

4.2 Exclusion criteria

- Serious somatic conditions (e.g., neurological disorders, stroke, head injury)
- Serious mental disorders (e.g., psychotic disorder, suicidality, substance use disorder, ADHD, developmental or intellectual disability)
- Impediment in hearing, vision, or language with an effect on testing
- Previous or planned bariatric surgery
- Use of medication that impacts weight or executive functioning (e.g., antipsychotics)
- Ongoing psychotherapy
- Pregnancy or lactation.

5 INDIVIDUAL STUDY PROCEDURE

5.1 Patient information and informed consent

Patients in behavioral weight loss treatment at the IFB Outpatient Unit will be informed about the study and screened for inclusion at the IFB Research Unit (telephone-based where consent has been given or in-person; see flowchart, Figure 1).

All patients will be comprehensively informed about the study in oral and written form at the baseline visit, giving them the opportunity to ask questions. Written informed consent will be obtained prior to randomization. The first original consent form will be kept at the study center and the second original consent form will be given to the participating patient.

5.2 Withdrawal of informed consent

Patients can withdraw their consent at any time point without any disadvantage. In this case, patients will be asked about the reason for withdrawal; however they do not need to provide this information. Information about the purpose and date of the patient's randomization and his/her withdrawal must remain in the documentation system. Confidentiality of patient's data will be protected by a documentation system working with anonymous patient codes.

5.3 Inclusion in the study

During screening which will be conducted via telephone or in-person, the following parameters will be assessed:

Time point	**Variable**
Screening Days -14 – -1	• Inclusion and exclusion criteria

If the patient meets all inclusion criteria and does not fulfil any of the exclusion criteria, he/she will be invited to a diagnostic visit (baseline visit). The baseline visit should not be conducted later than 14 days (2 weeks) after the screening.

At the beginning of the baseline visit, patients will be informed about the study, informed consent will be obtained, and inclusion/exclusion criteria will be re-assessed. The following parameters will be assessed during the baseline visit (all study arms):

Time point	**Variable**
Baseline (t0) Day 0	• Re-assessment of inclusion and exclusion criteria • Informed consent • Anamnesis • Comorbidities • Medication intake • Randomization • Anthropometry • Sociodemographics • Eating disorder psychopathology e.g., Eating Disorder Examination (EDE) • General psychopathology e.g., Patient Health Questionnaire (PHQ) • Executive functions e.g., Behavior Rating Inventory of Executive Functions (BRIEF-A) • Neuropsychological and brain activity-related measures e.g., Go/NoGo task

	• Behavioral measures e.g., Bogus taste test • Visual analogue scales (VAS): expectations, motivation

For randomization, the study team has to fill out a randomization form (R) and fax it to:

Center for Clinical Trials (ZKS Leipzig), data management **Fax: 0341 97 16 259**

Randomization will be conducted between 8:00am and 5:00pm on workdays. The study team at the IFB Research Unit will immediately receive the randomization result via email.

5.3.1 Assessment of violation of inclusion and exclusion criteria ex post

The violation of inclusion and exclusion criteria ex post does not generally result in excluding a patient from the study. In case that a randomized patient did not meet inclusion/exclusion criteria at the time of recruitment, the ZKS data management has to be informed as soon as possible. The principal investigator (Prof. Dr. Anja Hilbert) will decide about how to proceed with the patient in consultation with the project management (ZKS Leipzig). In any case, the documentation of the patient will be continued.

5.4 Description of the study procedure

Following the baseline visit including randomization (see 5.3), patients will receive active treatment or control (fNIRS neurofeedback/EEG neurofeedback) or delayed treatment which involves a period of 8 weeks without treatment. If a patient was randomized into the delayed treatment condition, the following variables will be assessed prior to the treatment 8 weeks after randomization:

Time point	**Variable**
Only delayed treatment **Before start of therapy** Week 8 (+ max. 2 weeks)	• Anamnesis • Comorbidities • Medication intake • Anthropometry • Sociodemographics • Eating disorder psychopathology e.g., Eating Disorder Examination (EDE) • General psychopathology e.g., Patient Health Questionnaire (PHQ) • Neuropsychological and brain activity-related measures e.g., Go/NoGo task • Behavioral measures e.g., Bogus taste test • Visual analogue scales (VAS): expectations, motivation

During treatment, all patients will be assessed weekly (i.e. at each treatment session), including the following variables:

Time point	Variable
During treatment, weekly Active treatments: Weeks 1-7 Delayed treatment: Weeks 9-15	• Brain activity-related outcomes e.g., EEG frequency band power • Visual analogue scales (VAS): state craving, liking, sense of control, hunger, satiety, and mood • Objective binge-eating episodes • (Serious) adverse events

The following variables will be assessed at the end of treatment, 8 (fNIRS neurofeedback and active control treatments) or 16 (delayed treatment control condition) weeks after randomization.

Time point	Variable
End of therapy (t1) Active treatments: Week 8 (max. + 2 weeks) Inactive control: Week 16 (max. + 2 weeks)	• Comorbidities • Medication intake • Randomization • Anthropometry • Sociodemographics • Eating disorder psychopathology e.g., Eating Disorder Examination (EDE) • General psychopathology e.g., Patient Health Questionnaire (PHQ) • Executive functions e.g., Behavior Rating Inventory of Executive Functions (BRIEF-A) • Neuropsychological and brain activity-related measures e.g., Go/NoGo task • Behavioral measures e.g., Bogus taste test • Visual analogue scales (VAS): expectations, motivation, and treatment evaluation

5.5 Follow-up

Six months after the end of treatment, all patients will be followed-up assessing the following variables:

Time point	Variable
Follow-up (t2) Month 6 (max. + 2 weeks)	• Comorbidities • Medication intake • Anthropometry • Sociodemographics • Eating disorder psychopathology

	e.g., Eating Disorder Examination (EDE) • General psychopathology e.g., Patient Health Questionnaire (PHQ) • Executive functions e.g., Behavior Rating Inventory of Executive Functions (BRIEF-A) • Behavioral measures e.g., Bogus taste test

5.6 Premature drop-out from treatment or follow-up

Every drop-out from treatment and/or follow-up will be documented by the study team and sent to the ZKS data center, including the exact date of withdrawal as well as the circumstances and reasons for withdrawal, as far as possible.

5.6.1 Discontinuation of the study intervention for individual patients

A patient may withdraw from the study at any time, at his or her own request, for any reason, specified or unspecified, and without penalty or loss of benefits to which the patient is otherwise entitled. Patients who have withdrawn from the study will not be allowed to re-enter later.

Furthermore, the responsible investigator has the right to discontinue the treatment of patients that experience one or more of the following incidents:

1. Adverse events (AE) or serious adverse events (SAE), particularly serious medical or psychological problems (e.g., cardiovascular disease, suicidal tendency, major depression) which do not allow any further treatment with the investigational intervention or which do not allow any further participation in the study because of impaired interpretability of the study results;
2. Reasons precluding attendance of scheduled visits;
3. Unacceptable benefit/risk ratio;
4. Lacking cooperation or compliance of the patient (i.e., intake of medication that is prohibited by the study protocol, intake of psychotropic or weight-affecting medications without indication, participation in psychotherapeutic interventions other than the study);
5. Refusal of the patient to continue participation.

The responsible investigator will make the decision about discontinuing treatment after contacting the coordinating investigator. Date of discontinuation, all recorded results at that time and, if known, the reasons for discontinuation are to be documented in the case report forms (CRFs). If possible, a final examination will be done. In any case, all patients will be followed up at each assessment time point after discontinuation, according to the intention-to-treat principle.

6 ADVERSE EVENTS (AE/SAE)

6.1 Adverse events and serious adverse events (AE/SAE)

6.1.1 Definition

The Declaration of Helsinki and the ICH-GCP Guideline E6 (point 4.11 and 5.17) set the protection of

participants in clinical trials in the first place. Therefore, the safety and harmlessness of interventions and therapies without drugs have to be proved in clinical trials.

The DIN EN ISO 14155:2011, section 3.2 defines adverse events (AE) as follows:

Adverse Events (AE) are

all in subjects, user or other persons occurring adverse medical events, unintended disease or injuries or undesirable clinical diagnoses (including abnormal laboratory results), regardless of whether these are related to the investigational product or not.

NOTE 1: Includes events associated with the test product or the comparison product.
NOTE 2: Includes events related to the procedure in question.
NOTE 3: For users or others persons the definition is limited to events associated with the test product.

Serious adverse events (SAEs) are according to § 2 No. 5 MPSV defined as follows:

"**Serious adverse event** is any problem encountered in a licensable clinical trial or a licensable performance evaluation unwanted event that has led directly or indirectly to death or to a serious deterioration in the health of a subject or user or any other person, could have led or could lead without regard to whether the event was caused by medical device; what has been stated applies to serious adverse events, which was issued in a clinical trial or performance evaluation for which an exemption from the permit requirement in § 20 paragraph 1 sentence 2 of the Medical Devices Act, have occurred."

DIN EN ISO 14155:2011, section 3.37 defines serous adverse events as follows and specifies what serious deterioration of the health status are:

An Adverse Event is defined to be serious if it:

a. resulted in death,

b. resulted in a serious impairment of health of the subject, either

- results in a life-threatening illness or injury, or
- results in a permanent disability of body structure or function, or
- requires in-patient hospitalization or prolongation of existing hospitalization, or
- results in a medical or surgical procedure in order to prevent a life-threatening illness or injury or a permanent injury to a body structure or function

c. is a congenital abnormality/birth defect.

NOTE: A scheduled hospitalization due to pre-existing conditions or requested by the CIP process, without a significant worsening in health is not considered a serious adverse event.

6.1.2 Documentation of adverse events (AE)

AEs will be documented at the AE form including the following information: start, end, description, date, intensity, causality, and consequence. The documentation of AEs will be realized for all intervention arms including the delayed treatment group during the study (from study inclusion to last follow-up visit).

Inpatient treatment of comorbidities, for example, a massive worsening of psychiatric symptoms, must be classified as SAEs and documented in the AE form.

6.1.3 Documentation of serious adverse events (SAE)

SAEs will be documented in the AE form, which contains additional questions for SAEs. At first, the original form remains at the study center. After the end of treatment (week 8 or 16, respectively) and

follow-up visit (month 6), the original AE form will be sent to the ZKS data management or handed to the monitoring staff together with all other case report forms. If additional information to the SAE are available at a later time point, they will be documented as well and sent to the ZKS data management or monitoring staff, respectively. SAEs will be documented during the patient's study period (from study inclusion to last follow-up visit). SAE involving patient's death will be immediately reported to the principal investigator. The study team will provide additional required information upon request. Confidentiality of patients' data will be protected by a documentation system working with anonymous patient codes. The primary notification as well as all following notifications of SAEs must be assignable to each other via the patient's identification number.

6.2 Device deficiency (DD)

6.2.1 Definition

Documentation and reporting of product deficiency, including serious product defects and events, is carried out as in clinical routine in accordance with the requirements of the MPSV §3. NeuroConn GmbH, Ilmenau, Germany (EEG) is thus responsible for examining occurred product defects and possibly related messages. Investigators and producers are responsible for reporting incidents to the competent authority.

Meets a defect the definition of SAEs, the documentation and reporting requirements described in section 6.1 should be considered.

6.3 Safety analyses

Every patient will be monitored closely regarding safety during the course of the study and includes the assessment of AEs and SAEs at the end of treatment (t1) and follow-up (t2). All AEs and SAEs will be analyzed descriptively in the final analysis.

6.4 Comorbidities

If an extreme worsening of the patient's mental health is noticed by the study therapist during neurofeedback sessions, short-term inpatient treatment should be considered. If admission to inpatient treatment is not considered necessary, two outpatient appointments outside the study schedule are allowed for crisis intervention. Neither inpatient nor outpatient treatment may be conducted by the study therapists. Inpatient treatment due to psychiatric reasons lasting more than one week will result in treatment drop-out/study discontinuation. Similarly, if the patient received two appointments for crisis intervention, the patient will be classified as treatment drop-out/non-completer (see paragraph 5.6.1).

6.5 Therapeutic actions

When the patient is in need for treatment due to an adverse event, the treatment/intervention must be applied according to current standards of medical research to rehabilitate patient's health. In medical emergency, appropriate equipment and medical products for reanimation have to be available, in order to treat the patient as quick as possible.

The treatment of AEs and SAEs must be documented.

In general	Regarding intervention
The initiated intervention must be documented at the respective place in the CRF and/or using additional records.	• Treatment interrupted • Treatment modified • Treatment not interrupted • Unknown • Not applicable

7 BIOMETRIC ASPECTS OF THE STUDY

7.1 Randomization algorithm

Randomization will be performed using an online tool programmed by the ZKS Leipzig (IFB Data centre).

The arm balance will be 1:1:1 and will be stratified by

- BMI (< 35.0 kg/m² vs. ≥ 35.0 kg/m²)
- sex
- behavioral weight loss treatment status

A minimization algorithm based on Pocock and Simon will be used.[57]

7.2 Endpoints

7.2.1 Primary endpoint

The number of objective binge-eating episodes (OBEs) over the past 14 days at post-treatment (t1), derived from the well-established Eating Disorder Examination interview, will be compared between groups, correcting for the baseline value. OBEs are consistently reported as the primary outcome measure in BED treatment trials.

7.2.2 Secondary endpoints

(a) Feasibility (between t0-t1): Recruitment, attrition, assessment completion, compliance, patients' program evaluation

(b) Number of OBEs (t0, t2), remission from objective binge eating (EDE) (t0-t2), eating disorder psychopathology (EDE-Q) (t0-t2)

(c) Neuropsychological and neurophysiological outcomes (t0, t1): e.g., inhibition (Go/NoGo task)

(d) Weight management-related behaviors (t0-t2): e.g., self-efficacy (GSES)

(e) Mental health (t0-t2): e.g., depressive symptoms (PHQ-D)

(f) Physical health (t0-t2): e.g., body mass index (kg/m²)

7.3 Statistical description of the trial hypothesis

This clinical trial evaluates whether neurofeedback results in fewer objective binge-eating episodes after

end of treatment (i.e., 2 months after randomization) than a delayed treatment group. Furthermore fNIRS neurofeedback, EEG neurofeedback, and delayed treatment will be compared.

7.4 Sample size

7.4.1 Estimates of effects

Two clinical trials by the same group analyzed the effects of EEG neurofeedback on binge eating and found effect sizes of 0.64 and 0.65[29,30]. Preliminary data for BED showed an effect size within a treatment group of 0.40 [32].

7.4.2 Statistical error terms

The level of significance is set at $\alpha = 5\%$, aiming for a power of $1 - \beta = 80\%$.

7.4.3 Drop-outs

A drop-out rate of 15% was observed in an EEG neurofeedback trial with a follow-up 3 months after end of treatment.[30] Based on these data and our own experience we assume a dropout rate of 20%. Although dropped-out from treatment, patients who discontinued treatment will be assessed at later assessment time points, if possible.

7.4.4 Sample size calculation

Based on a conservative effect size of 0.55 (compared to 0.65 quoted above), a t-test will have 80% power if 63 patients are analyzed (42 in the pooled intervention groups and 21 in the waiting control group), as determined using the software PASS 11. The width of the confidence intervals for the difference in means between two groups can then be expected to be about 0.88 SD for the pooled variance. The covariates incorporated into the analysis methods mean that the true power can be expected to be somewhat higher than that of the t-test reported here.

Taking into account a drop-out rate of about 20%, a total of 78 patients (26 per group) will be randomized.

7.5 Statistical methods

7.5.1 Analysis population

Analysis of the primary and secondary outcomes are based on the full analysis set (FAS). Further, the analysis of the primary outcome will be performed in the per-protocol set (PPS) to evaluate the treatment effect for patients with good protocol adherence, if FAS and PPS comprise a sufficiently different set of patients. For safety analysis, adverse events and SAEs will be analyzed descriptively.

The FAS includes all patients who were randomized. Every attempt will be made to acquire missing data for the primary outcome.

The PPS includes all patients of the FAS without serious violations against the study protocol. The following protocol violations will be classified as serious:

- At least one inclusion or exclusion criterion was not met.

- Treatment was not conducted as mandated, that is:

    - Temporal delay of at least one treatment session by 2 weeks of the planned date (based on the date of the first treatment session)

- Absence of more than 6 of the planned 12 treatment sessions

- Intake of forbidden medications

- Psychological treatment during study participation

Further serious protocol violations will be specified in the data analytic plan, if necessary.

7.5.2 Planned methods for analysis

Primary analysis: The primary endpoint, the number of OBEs at post-treatment (t1) ~~and pre-treatment (t0)~~, will be investigated using ANCOVA with OBEs at t1 as the dependent variable, OBEs at t0 as a covariate as well as the stratification criteria. A closed-testing procedure will be used, meaning that the initial comparison will be between the two intervention groups combined and the waiting group and the three pair-wise tests (fNIRS vs. waiting group, EEG vs. waiting group and fNIRS vs. EEG) will be performed without adjustment if the global test is significant.[58,59] The analysis will follow the intent-to-treat principle and will be based on the full analysis set. Every attempt will be made to acquire missing data. If data missing for the primary outcome can be expected to bias results in a meaningful way, multiple imputation will be performed. Further, the analysis of the primary outcome will be performed in the per-protocol set to evaluate the treatment effect for patients with good protocol adherence.

Secondary analyses: Recruitment and attrition rates will be described quantitatively and a qualitative analysis of the hurdles involved in recruitment and in maintaining patient commitment will be presented. Further secondary outcomes will be analyzed in an exploratory, descriptive manner, and will be evaluated presented with 95% CIs, as well as parametric or non-parametric tests, depending on the scale level and type of distribution of the observed variables. Multiple comparisons given three arms will be taken into account using e.g. Dunnett's test or Tukey's Honest Significant Differences and where all pair-wise comparisons will be made, independent of the result of a global test. Maintenance of treatment success over time will be evaluated. Predictors of treatment outcome will be identified using regression analyses.

7.6 Statistical monitoring

The structure of the trial is fairly simple, i.e. there are a small number of visits at which primarily psychological measures will be obtained, often questionnaires and structured interviews. As such, statistical monitoring will focus on a small number of key issues, including

- missing data
- drop-outs and the proportion in each arm
- timing of visits
- number and timing of therapy sessions.

7.7 Interim analysis

No interim analysis will be performed.

7.8 Final analysis

The final analysis will be performed after the last patient has terminated the trial, all database queries have been resolved and the database has been locked.

8 ETHICAL CONSIDERATIONS

8.1 GCP-declaration

The trial will be conducted in accordance with the guidelines for Good Clinical Practice (GCP). All involved parties of the study (principal investigator, study and data management, study team) commit themselves to the Declaration of Helsinki (Version Sommerset West 1996), as well as all pertinent national laws and the ICH Guideline for Good Clinical Practice (GCP) E6 issued in June 1996 and CPMP/ICH/ 135/95 from September 1997.

8.2 Ethical approval

According to the specifications of §15 of the German federal Medical Association's professional code of conduct, ethical approval of the study will be sought at the responsible ethics committee (Ethics Committee of the University of Leipzig).

8.3 Supplementary changes of the study protocol

Changes in the study protocol must be reported to the Ethics Committee of the University of Leipzig and, where necessary, a new vote has to be gathered. Changes needing a positive vote may only be realized after the Ethics Committee of the University of Leipzig agreed with these changes.

Changes that require the vote of the Ethics Committee of the University of Leipzig are associated with one or more of the following aspects:

- Essential changes in treatments
- Reappraisal of patient risks
- Additional assessments or analyses that warrant changes of the patient education and consent form
- Changes that affect the management and conduct of the study substantially.

9 DOCUMENTATION

9.1 Patient identification list

All patient-related data will be documented in a pseudonymized format. Therefore, a pseudonym will be used with which the patient’s identity cannot be inferred from alone. The assessor keeps a patient identification list (PIL) which includes the patient identification number, the patient’s name and birth date. The PIL must be treated with absolute confidentiality, must not leave the study center and has to be archived for at least 10 years after the end of the study. In addition, the patient’s participation in the study must be documented in the patient’s record.

9.2 Case Report Forms (CRF)

Case report forms (CRF) will be designed by the ZKS data management in close cooperation with the study group.

The CRF for collection the clinical data will be provide to the trial center as electronic form (eCRF). Authorized members of the study team for this task will connect to the database via internet and input

data directly into the SecuTrial database via eCRF data entry masks. In order to facilitate the documentation as per protocol in case of malfunction of the electronic system or any of its components, a paper version of the clinical CRF will be additionally provided. The content of this paper version will be transferred to the eCRF as soon as the electronic system is available again. The eCRF will be completed shortly after each study visit.

Each CRF page of the clinical part will be signed electronically by an authorized member of the study group. This confirms that all data on the eCRF are correct and have not been changed. If a value gets changed on the eCRF later the eCRF has to be signed again. This ensures that changes on the eCRF will be dated and signed as well. All entries and data changes will be tracked automatically including date, time and person who entered/changed information (audit trail). Corrections and major missing data have to be explained.

If the investigator authorizes other members of the study team to enter and sign CRF data, their name, initials, position, signature must be documented via Staff Signature und Delegation Log.

However, the investigator has final responsibility at all times for the accuracy and authenticity of all clinical and laboratory data entered in the CRF.

The psychological measures are provided to the trial center as a copy template. The ZKS Leipzig data management receives the original CRF, while the trial center is in charge to make a copy of the CRF which remains at the trial center. These will be entered into the eCRF by ZKS Leipzig staff afterwards.

Documentation at the paper-based CRF must be performed using a dark pen. For corrections, the incorrect data entry must be crossed out using a horizontal line so that the initial entry remains visible. The correction must be confirmed by initials and current date by authorized study staff. It is not allowed to use corrections fluids.

Signature at the CRF confirms the correctness of data and possible corrections.

After the t1 diagnostic session (8 or 16 weeks after randomization, respectively), all original CRFs will immediately be send to the ZKS Leipzig data management or collected by the monitor for data entry and analysis. Similarly, CRFs of the t2 follow-up visits (6 months after end of treatment) will be promptly sent to the ZKS Leipzig data management or collected by the monitor.

All data which are provided in the patient record are considered as source data.

9.3 Data management

All study data will be collected in the Clinical Data Management System (CDMS). The EDC Tool SecuTrial by InterActive will be used. The database will be validated according to the Standard Operating Procedures (SOPs) of the ZKS Leipzig - KKS prior to data capture.

The information entered into the database by the data management team of the ZKS Leipzig is systematically checked for completeness, consistency and plausibility by routines implemented in the CDMS. Error messages generated by these routines will be checked by the data management staff. Queries obviously not representing a problem will be closed. Errors with an obvious solution will be corrected by the staff of the ZKS Leipzig immediately (self-evident correction).

Discrepancies, errors or omissions will be passed to the investigator or an authorized member of the study team at the investigational site by the CDMS. The investigator will receive notification of all queries concerning his/her investigational site. The ZKS Leipzig will supervise and support the solution of the queries. Corrected data will be re-checked by automatic routines after entry. In case a query cannot be solved or closed by the investigator or designated study staff, the data management staff of the ZKS Leipzig may close the query. This shall happen in agreement with the study biometrician and

clarification, if the information addressed by the query is relevant for the results of the study, or not.

During the whole course of the study, a backup of all data is made on a daily basis. Unauthorized access to patient data is prevented by the access concept of the CDMS which is based on a strict hierarchy and role model. Any change of data (e.g. when data is changed in the CDMS during query management) is recorded automatically via audit trail within the CDMS.

At the end of the study, once all data in the CDMS have been declared complete and accurate, the trial will be locked in the CDMS. Thereafter, any changes to the data are possible only by joint written agreement between coordinating investigator, biometrician and data manager.

9.4 Archiving

All relevant study documents (trial master file), electronically derived data, the original CRFs and the final study report will be stored for at least 10 years at the ZKS Leipzig after trial completion.

At the study center, the investigator site file, the patient identification list, the signed informed consent forms, copies of CRFs, and the patient records will be stored for at least 10 years after the trial completion.

10 MONITORING OF THE CLINICAL TRIAL

10.1 Access to source data

Due to legal regulations for the protection of data quality and monitoring of the conduct of the study, the assessors are obligated to allow inspection of patient records (source data) to authorized third parties including monitors, auditors, and other authorized persons of the customer. These persons are obliged to secrecy.

10.2 Monitoring

Monitoring will follow ICH-GCP guidelines and includes one initiation visit, one interim visit, and one close-out visit. For all patients, the informed consent documents will be checked. In addition, source data verification of the key data will be performed in a random sample of a portion of the patients. Monitoring will follow the ZKS SOPs.

10.3 Independent monitoring of the study

Because of the small scope of this study, an independent Data Monitoring and Safety Committee (DMSC) was not deemed to be necessary. In case that a patient shows increased psychological distress during treatment, a clinical psychologist from the IFB Outpatient Unit will offer crisis intervention.

11 DATA SAFETY AND CONFIDENTIALITY

In the context of the study, personal data of the patient including information about the treatment and course of disorder are assessed. These data are saved electronically and analyzed in a pseudonymized format (i.e., without explicit reference to the patient name) using an identification number.

Because it is necessary to contact patients directly, the name and address/telephone number of the patient are documented and saved after gathering written informed consent of the patient. These data are stored separately from the study data. Inference can be made using the patient identification number.

Data entry and processing take place at the ZKS Leipzig where a security concept guarantees protection against unauthorized access and data loss. In addition, the ZKS Leipzig is responsible for keeping the legal requirements of data protection. Study data are protected from unauthorized access and only study personal are allowed to access the data. The study personnel is obliged to secrecy.

In case that a patient withdraws informed consent, it will be checked whether the saved data are still required. Data that will not be required anymore will immediately be deleted. All assessed data will be deleted after the study objective was achieved/after finishing associated projects, or by 10 years, if not legal, statutory, or contractual periods of retention conflict.

Declaration of data protection

Regarding data entry, processing, and analysis, which take place at the ZKS Leipzig, University of Leipzig, all legal regulations of data protection will be meet. Study data are protected from unauthorized access and only study personal are allowed to access the data. The study personnel is obliged to secrecy.

12 ADMINISTRATIVE REGULATIONS

12.1 Study conduct according to the study protocol

The proposed clinical trial will be planned, conducted, and analyzed according to the requirements of the ICH-GCP and legal regulations.

Violations against the study protocol include all deviations from instructions and procedures as described in the study protocol. These are:

- Missing assessments/visits or malapropos assessments/visits, for example, not meeting the number of minimum treatment sessions
- Lack of compliance
- Intake of forbidden medication
- Screening failure (patient was randomized erroneously, i.e., inclusion criteria were not met or exclusion criterion was present)
- Concurrent psychotherapy (inpatient treatment lasting > 1 week or > 2 outpatient appointments for crisis intervention)
- Inpatient treatment due to other reasons lasting > 2 weeks

After a patient was included in the study, the assessor bears responsibility for avoiding protocol violations to retain the patient in the study.

Serious violations from the study protocol will immediately be reported to the principal investigator. All violations from the study protocol will be documented and discussed with the responsible biometrician prior to analysis.

The assessor has to make sure that all data were documented according to the study protocol. Small deviations cannot be avoided in everyday working life, but must be documented well grounded.

12.2 Funding and insurance

The study is funded by the German Federal Ministry of Education and Research (grant 01EO1501).

A patient insurance is not proposed as there is no use of medication or medical products. Instead, the trial includes a neuropsychological intervention for which patient and travel accident insurances are not necessary.

12.3 Publication agreement and registration

This trial is to be published in internationally accepted journals. The PI, Prof. Anja Hilbert, will make any effort for publishing the results of the study, independent from the direction of the study outcome.

Prof. Dr. Anja Hilbert will be the first author. As co-authors, psychological or medical staff of the working group Behavioral Medicine, the University Medical Center Leipzig, cooperating partners, and the biometrician of the IFB data center will be considered, following established guidelines for authorship.

The authors are obliged to cite the IFB AdiposityDiseases. For institutional assignment, authors should use “University of Leipzig Medical Center, IFB AdiposityDiseases”.

In all publications the BMBF must be acknowledged as follows:

“The study was funded by the German Federal Ministry of Education and Research (grant 01EO1501).”

Similarly, the funding institution and the IFB AdiposityDiseases must be mentioned for citable abstracts. On posters, the logos of the IFB AdiposityDiseases and the BMBF must be used in addition.

The study will be registered in a public study register, for example, the German Clinical Trials Register (DRKS), prior to the start of recruitment.

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14 SIGNATURE TO THE STUDY PROTOCOL

Acknowledgement of the study protocol

The final version of the study protocol is certified hereby:

Principal investigator	18.01.2018	
	Date	Signature
Biometrician:	18.01.2018	
	Date	Signature

15 ACCEPTANCE OF THE STUDY PROTOCOL

Hereby, I confirm that I read, understood, and accept all parts of the present study protocol. I agree to take care that all included patients will be treated, observed, and documented according to the specifications as determined in the study protocol. I agree to take care that all individuals involved in the study are informed about the content of the study protocol.

Date: _____

Signature principal investigator: _____

Adress (Prüfzentrum):

University of Leipzig Medical Center
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Behavioral Medicine
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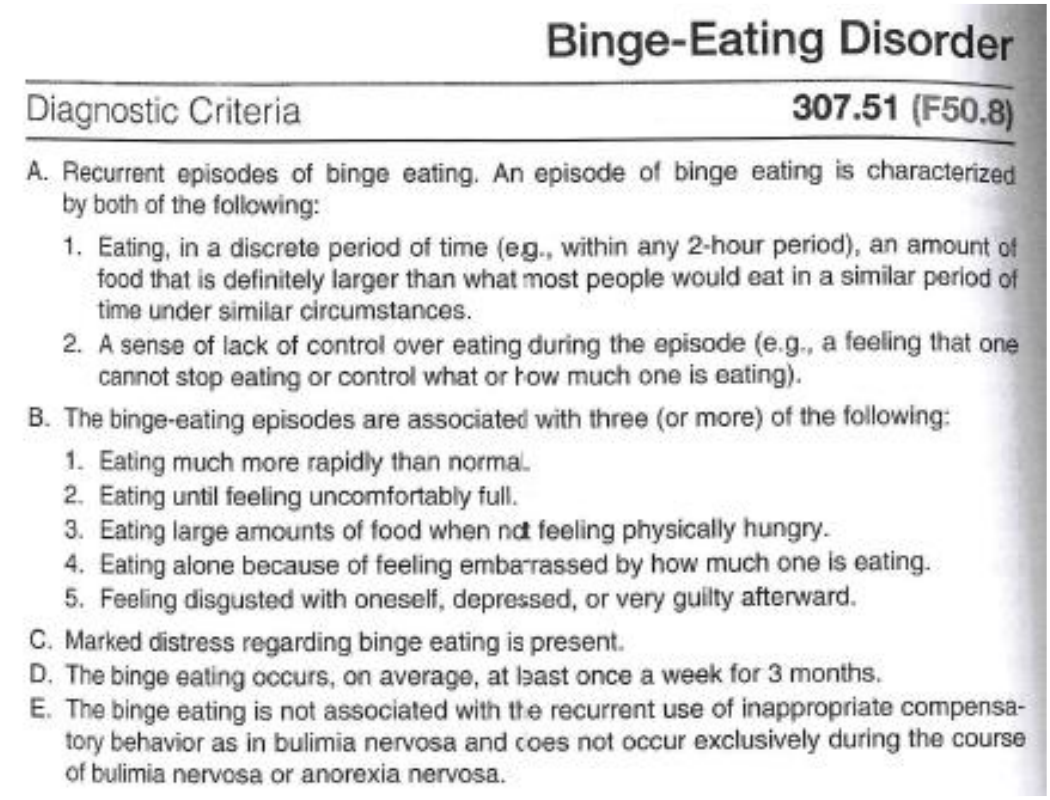
04103 Leipzig

16 APPENDIX

16.1 Definitions

American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, 5th ed.; DSM-5. Washington, DC: APA, 2013.



Binge-Eating Disorder

Diagnostic Criteria **307.51 (F50.8)**

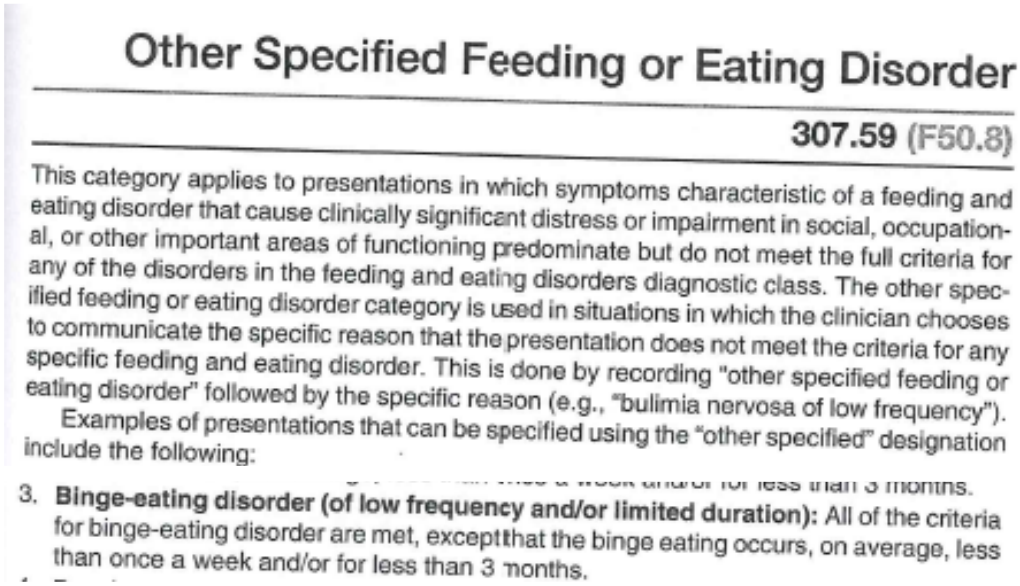
A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   1. Eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than what most people would eat in a similar period of time under similar circumstances.
   2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).

B. The binge-eating episodes are associated with three (or more) of the following:
   1. Eating much more rapidly than normal.
   2. Eating until feeling uncomfortably full.
   3. Eating large amounts of food when not feeling physically hungry.
   4. Eating alone because of feeling embarrassed by how much one is eating.
   5. Feeling disgusted with oneself, depressed, or very guilty afterward.

C. Marked distress regarding binge eating is present.

D. The binge eating occurs, on average, at least once a week for 3 months.

E. The binge eating is not associated with the recurrent use of inappropriate compensatory behavior as in bulimia nervosa and does not occur exclusively during the course of bulimia nervosa or anorexia nervosa.



Other Specified Feeding or Eating Disorder

307.59 (F50.8)

This category applies to presentations in which symptoms characteristic of a feeding and eating disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet the full criteria for any of the disorders in the feeding and eating disorders diagnostic class. The other specified feeding or eating disorder category is used in situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for any specific feeding and eating disorder. This is done by recording "other specified feeding or eating disorder" followed by the specific reason (e.g., "bulimia nervosa of low frequency").

Examples of presentations that can be specified using the "other specified" designation include the following:

3. **Binge-eating disorder (of low frequency and/or limited duration):** All of the criteria for binge-eating disorder are met, except that the binge eating occurs, on average, less than once a week and/or for less than 3 months.

16.2 Abbreviations

ADHD	attention deficit-/hyperactivity disorder
AE	adverse event
BED	binge-eating disorder
BMI	body mass index
BWL	behavioral weight loss
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
EEG	electroencephalography
EK	ethical commission
FAS	full analysis set
fMRI	functional magnetic resonance imaging
fNIRS	functional near infrared spectroscopy
GCP	good clinical practice
GCP-V	GCP-regulation
ICH	International Conference on Harmonisation
IFB	Integrated Research and Treatment Center AdiposityDiseases
OBE	objective binge-eating episode
PET	Positron Emission Tomography
PIL	patient identification list
PPS	per-protocol set
ROI	region of interest
SAE	serious adverse event
SOP	standard operating procedure
ZKS Leipzig	Zentrum für Klinische Studien Leipzig (Clinical Trial Centre Leipzig)
WL	waiting list
WLM	weight loss maintenance